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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/486,070	06/07/95	STAVRIANOPOULOS	J ENZ-7 (P) (C3)

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EXAMINER
MARSCHEL, A

ART UNIT	PAPER NUMBER
	1631

DATE MAILED:

10/10/95

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No. 08/486,070	Applicant(s) Stavrianopoulos et al.
Examiner Ardin Marschel	Art Unit 1631

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on as listed in action attached
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle* 1035 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 718-1265 is/are pending in the application.
- 4a) Of the above, claim(s) _____ is/are withdrawn from consideration.
- 5) Claim(s) as listed as attached is/are allowed.
- 6) Claim(s) as listed as attached is/are rejected.
- 7) Claim(s) as listed as attached is/are objected to.
- 8) Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are objected to by the Examiner.
- 11) The proposed drawing correction filed on _____ is: a) approved b) disapproved.
- 12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) All b) Some* c) None of:

1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. _____.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

- 14) Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- 15) Notice of References Cited (PTO-892) 18) Interview Summary (PTO-413) Paper No(s). _____
- 16) Notice of Draftsperson's Patent Drawing Review (PTO-948) 19) Notice of Informal Patent Application (PTO-152)
- 17) Information Disclosure Statement(s) (PTO-1449) Paper No(s). 6 sheets 20) Other: _____

Claims status list for 08/486,070 for 10/5/01.

Pending claims are 718-1265.

There are no allowed claims.

Rejected claims are 718-874, 878-880, 882, 883, 886, 890-892, 894, 895, 901, 903-917, 924-957, 961-963, 965, 971, 973-987, 994-1028, 1032-1034, 1036, 1040, 1044-1046, 1048, 1049, 1055, 1057-1060, 1062-1071, and 1078-1265.

Objected to claims are 875-877, 881, 884, 885, 887-889, 893, 896-900, 902, 918-923, 958-960, 964, 966-970, 972, 988-993, 1029-1031, 1035, 1037-1039, 1041-1043, 1047, 1050-1054, 1056, 1061, and 1072-1077.

Applicants' arguments and amendments, filed 3/12/01, 4/26/01, 5/8/01, 5/10/01, 5/30/01, 6/7/01 and 6/11/01; have been entered and have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

The amendment, filed 5/8/01, is objected to under 35 U.S.C. § 132 because it introduces new matter into the specification. 35 U.S.C. § 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: The newly submitted abstract, filed 5/8/01, broadens the array concept over the instant disclosure as filed to include any array of substrate surfaces. As also summarized in detail below, all disclosures of arrays instantly as filed were narrower in that they also required separate hybridization solution and/or mixtures at each different substrate location which is a narrower limitation as compared to the unlimited array type presently set forth in the submitted abstract.

Applicant is required to cancel the new matter in the response to this Office action.

Claims 718-872, 903, 906, 907, 973, 976, 977, and 1111-1265

are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

A thorough review of the instant application had previously revealed that several of the claims contain NEW MATTER which was not disclosed as filed and was summarized in the previous office action, mailed 9/7/00, and is reiterated and maintained here.

In claims 718-872 and 1111-1265 generic arrays are claimed. These claimed arrays start with the broadest versions in claims 718 and 1111 as only requiring a substrate surface with double-stranded nucleic acid fixed or immobilized thereto with at least one strand labeled as described in said claim. The closest array description, as filed, is given in the specification on page 16, lines 9-27. In this description the array also is limited to glass plates having depressions or wells with denatured analytes deposited therein, wherein single stranded analytes are fixed to the surfaces of the wells. Chemically labeled probes may then be hybridized to these analytes and subjected to detection of any probe-analyte hybrid. It is noted that the analytes are characterized as being "various" which supports the presence of "different" analytes deposited in each well or depression. It is additionally noted that plastic wells are a disclosed option as

given in the bridging sentence between pages 20 and 21 of the instant specification. Polystyrene microfilter wells are described on page 22, lines 10-12, as a solid support. The practice of fixing polynucleotide analytes to conventional microtiter plates is described on page 23 at the start of Example 7. In summary, the array embodiments, as filed, are all at least directed to solid supports with wells or depressions therein. It is lastly noted that instant claims 718 and 1111 do not require either wells or depressions as being the form of the array of analyte fixation sites nor its being either glass or plastic, wherein microtiter arrays are deemed to be made of plastic. Such broader array embodiments which are NEW MATTER, for example, include flat surface arrays or non-glass or non-plastic arrays. Applicants have cited a multitude of passages from the instant application as filed but not one broadens the array practice to that which is claimed and indicated above as thus containing NEW MATTER. It is also noted that the Declaration of Dr. CHERYL H. AGRIS has been reviewed and supports the concept of a solid support with well etc. as has been noted before as having support as filed. However, nowhere in this Declaration has there been pointed to the broadening of array practice wherein "ONE" hybridization fluid or mixture simultaneously washes over all, or even a plurality, of the wells or depression on such array surfaces. That is, wherever an array of wells etc. are describe

each well or depression etc. forms its own hybridization reaction mixture. Again there is no array practice disclosed as filed for "ONE" hybridization fluid or mixture contacting, flowing over, or in any way simultaneously permitting overall array hybridization. Contrary to Declarant's allegations wishing to reduce the essential nature of this array practice broadening, the application, taken as a whole or in detail focuses cleanly on separate hybridization reaction mixtures wherever this level of detail is described and thus is essential regarding the scope of the disclosure of this issue.

Several of the instant claims contain the limitation given as "glass-coated". This limitation is NEW MATTER in that glass-coated indicates a solid support which has a coating of glass over it. This coating type has not been found as filed. It is noted that coatings of various types are instantly disclosed such as coating of a solid support with a material which permits linkage, fixation, or immobilization of analytes, for example. Thus, the coating is not glass per se but rather optionally a linker coating on a glass solid support. The phrase "glass-coated" is indicative of a solid support having a glass coating thereon which is NEW MATTER in instant claims 724, 802, 875, 887, 958, 1029, 1041, 1117, and 1195. Applicants argue that a coating on a glass or plastic slide during an assay overcomes this rejection. This is non-persuasive because such a coating is

limited to coating on glass or plastic and not the generic glass-coated or plastic-coated limitation which includes coating on glass or plastic as well as glass or plastic as a coating on another material.

Several of the instant claims contain the limitation given as "plastic-coated". This limitation is NEW MATTER in that plastic-coated indicates a solid support which has a coating of plastic over it. This coating type has not been found as filed. Thus, similar to the above glass-coated NEW MATTER, the plastic-coated NEW MATTER is present in instant claims 727, 805, 878, 890, 961, 1032, 1044, 1120, and 1198. Applicants argue that a coating on a glass or plastic slide during an assay overcomes this rejection. This is non-persuasive because such a coating is limited to coating on glass or plastic and not the generic glass-coated or plastic-coated limitation which includes coating on glass or plastic as well as glass or plastic as a coating on another material.

Several of the instant claims contain the limitation given as "oncogene" or combination thereof containing an oncogene. This limitation is NEW MATTER in that the limitation, oncogene, has not been found as filed. The amendment, filed 5/8/01, referred to the reference EP 63879 for support for these limitations. The next paragraph, below, explains why this is improper incorporation by reference and supports this rejection.

The following claims contain this NEW MATTER: 743, 819, 906, 976, and 1136.

Several of the instant claims contain limitation directed to specific types of mutations given as deletion, insertion, inversion, point mutation, and a combination thereof. These limitations are NEW MATTER in that the limitations have not been found as filed. It is noted that the amendment, filed 5/8/01, indicated that these mutation types could be found in the publication EP 63879, cited on pages 9 of the instant specification. Consideration of this page 9 citation reveals that it was cited as a reference which indicated mutations but no more detailed limitations. It was not cited for any other disclosure. This is an incorporation by reference of pointed to subject matter but not other subject matter. Such incorporations by reference must be directed to particular disclosures for them to be usable for giving written basis for claim limitations. A specific claim limitation is clearly essential subject matter. It is improper to incorporation by reference essential subject matter cited in a foreign patent application. It is improper to generically cite such a reference and then utilize it for anything therein without defining in the citation what it is cited for. In this case the publication was cited for non-radioactive signalling etc. review and not for mutation types. Thus, it does not serve as a proper basis for incorporating

mutation types into the instant claims. For further discussion, see the M.P.E.P. at section 608.01(p), part I, subsection A. The following claims contain this NEW MATTER: 744, 820, 907, 977, and 1137.

Several of the instant claims contain the limitation given as "partially double-stranded". This limitation is NEW MATTER in that the limitation has not been found as filed. In the amendment, filed 5/8/01, applicants indicate the "double-stranded" inherently gives written basis for this limitation. This is not deemed to be persuasive as double-stranded lacks any specificity such as partial character for this limitation. The following claims contain this NEW MATTER: 740, 816, 903, 973, and 1133.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 873, 874, 878-880, 882, 883, 886, 890-892, 894, 901, 903-906, 908-917, 924-957, 961-963, 971, 973-976, 978-987, 994-1028, 1032-1034, 1036, 1040, 1044-1046, 1048, 1055, 1057-1060, 1062-1071, and 1078-1110 are rejected under 35 U.S.C. § 102(b) as being clearly anticipated by Kourilsky et al. (UK 2,019,408).

This rejection is reiterated as necessitated by amendment regarding newly added claims. Applicants argue that photometric means is now in the claims and not in the reference. In response the enzymatic detection of the reference generates a colored dye reaction which is clearly photometrically detected. As previously described of record Kourilsky et al. discloses the centrifugal fixation of a target/probe hybrid with a chemical label thereon on page 3, lines 18-54, with evaluation of bound probe via a β -galactosidase in solution of the resuspended hybrids. The quantitation limitations in instant claims are a capability which clearly is present considering the solution enzyme determination of Kourilsky et al. and thus is anticipated by the reference, even though Kourilsky et al. does not perform the quantitation while the hybrids are still fixed on the support. Also, centrifuge tubes for such a centrifugal procedure are well known to be made of translucent, non-porous, plastic. Several added instant limitations directed to various bridging moieties and immobilization via hybridization of the probe are deemed anticipated by the somewhat complex assemblage of the

probe/target hybrid and label moieties in that portions are direct, portions are indirect, etc. The probe is clearly immobilized via hybridization. Otherwise the assay would be non-functional if non-hybridized probe also was fixed by the centrifugation step.

Claims 873, 874, 878-880, 882, 883, 886, 890-892, 894, 895, 901, 903-906, 908-917, 924-957, 961-963, 965, 971, 973-976, 978-987, 994-1028, 1032-1034, 1036, 1040, 1044-1046, 1048, 1049, 1055, 1057-1060, 1062-1071, and 1078-1110 are rejected under 35 U.S.C. § 102(e) as being clearly anticipated by Stuart et al. (P/N 4,732,847) or Ward et al. (P/N 4,711,955).

This rejection is reiterated as necessitated by amendment. Again applicants argue that photometric means is not in the reference and again this is non-persuasive as fluorescent detection is clearly a photometric means of detection. Stuart et al. discloses the practice of in-situ hybridization on a coverslip with fluorescent antibody detection of probe/target hybrids in column 6, lines 17-57, which anticipates the above instant claims. The target samples were prepared on acid washed microscope slides as indicated in column 4, lines 61-67. The slides and coverslips at the time were well known to be transparent glass and non-porous and form a system. The acid washing is deemed a surface treatment. The fluorescent labeling is deemed a type of chemical label because instant dependent

claims includes fluorescent labeling in the signalling limitations. It is noted that Stuart et al. does not disclose quantitation of signal but it is also noted that the instant claims are directed to a capability for quantitation of label and are not method claims. A fluorescent label as utilized in Stuart et al. emits light which is well known to be quantifiable and thus anticipates the instant claims listed above. See the below paragraph which cites legal decisions as to shifting the burden to applicants to distinguish the reference disclosure over the invention when the claimed subject matter is expected to anticipate the claimed invention by having properties cited in the instant claims but not measured in a cited prior art reference. Ward et al. also cites in-situ hybridization with detection with avidin-peroxidase in columns 19-20 therein which reads on the above claims also due to the quantifiability of such signals.

It is noted that In re Best (195 USPQ 430) and In re Fitzgerald (205 USPQ 594) discuss the support of rejections wherein the prior art discloses subject matter which there is reason to believe inherently includes functions that are newly cited or is identical to a product instantly claimed. In such a situation the burden is shifted to the applicants to "prove that subject matter shown to be in the prior art does not possess characteristic relied on" (205 USPQ 594, second column, first

full paragraph).

The disclosure is objected to because of the following informalities:

In claim 736 and several other claims the word "expoxy" appears to be misspelled.

Appropriate correction is required.

No claim is allowed.

Applicants' amendment necessitated the new grounds of rejection. Accordingly, **THIS ACTION IS MADE FINAL**. See M.P.E.P. § 706.07(a). Applicants are reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The CM1 Fax Center number is either (703) 308-4242 or (703) 305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ardin Marschel, Ph.D., whose telephone number is (703) 308-3894. The examiner can normally be reached on Monday-Friday from 8 A.M.

Serial No. 08/486,070

- 13 -

Art Unit: 1631

to 4 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on (703)308-4028.

Any inquiry of a general nature or relating to the status of this application should be directed to Patent Analyst, Tina Plunkett, whose telephone number is (703)305-3524 or to the Technical Center receptionist whose telephone number is (703) 308-0196.

October 5, 2001

Ardin H. Marschel
ARDIN H. MARSCHEL
PRIMARY EXAMINER